

### AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A process for determining the level of a membrane transport protein translocated to the plasma membrane of a cell, said ~~method~~process comprising:
  - (a) determining the level of a membrane transport protein at the plasma membrane of the cell using a method comprising:
    - (i) contacting the cell with a ligand that binds to an extracellular domain of the membrane transport protein for a time and under conditions sufficient for the ligand to bind to the membrane transport protein at the plasma membrane of the cell; and
    - (ii) determining the level of ligand bound to the membrane transport protein;
  - (b)
    - (i) permeabilizing or disrupting the plasma membrane of a cell and contacting the membrane transport protein within the cell with the ligand for a time and under conditions sufficient for the ligand to bind to the membrane transport protein; and
    - (ii) determining the level of ligand bound to the membrane transport protein; and
  - (c) comparing the level of ligand determined at (a) (ii) and (b) (ii) to determine the level of the membrane transport protein at the plasma membrane relative to the level of the membrane transport protein inside the cell.
2. **(Original)** The process according to claim 1 wherein the membrane transport protein is a glucose transport (GLUT) protein.
3. **(Original)** The process according to claim 2 wherein the membrane transport protein is GLUT4.
4. **(Cancelled)**
5. **(Original)** The process according to claim 2 wherein the membrane transport protein is GLUT1.
6. **(Cancelled)**
7. **(Original)** The process according to claim 1 wherein the membrane transport protein is a mutant membrane transport protein having a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein.

8. **(Cancelled)**
9. **(Cancelled)**
10. **(Cancelled)**
11. **(Original)** The process according to claim 1 wherein the membrane transport protein is labeled to facilitate binding of the ligand to the membrane transport protein.
12. **(Cancelled)**
13. **(Cancelled)**
14. **(Currently amended)** The process according to claim ~~13~~11 wherein the label comprises influenza virus hemagglutinin (HA) (SEQ ID NO: 15).
15. **(Cancelled).**
16. **(Cancelled)**
17. **(Cancelled)**
18. **(Cancelled)**
19. **(Cancelled)**
20. **(Cancelled)**
21. **(Cancelled)**
22. **(Original)** The process according to claim 1 wherein the ligand capable of binding to the membrane transport protein is an antibody.
23. **(Cancelled)**
24. **(Cancelled)**
25. **(Cancelled)**
26. **(Cancelled)**
27. **(Currently amended)** The process according to claim 1 wherein the plasma membrane is permeabilized or disrupted by contacting the plasma membrane with an agent that permeabilizes or disrupts a membrane for a time and under conditions sufficient for permeabilization or disruption to occur.
28. **(Cancelled)**
29. **(Cancelled)**
30. **(Original)** The process according to claim 1 wherein the level of the ligand bound to the membrane transport protein is determined by a process comprising contacting the ligand

with an antibody that specifically binds to the ligand for a time and under conditions sufficient for an antibody-antigen complex to form and determining the level of the complex wherein the level of the complex indicates the level of the ligand bound to the membrane transport protein.

31. **(Cancelled)**

32. **(Currently amended)** The process according to claim 1 ~~or 30~~ wherein the level of the ligand bound to the membrane transport protein is determined using a fluorescence linked immunosorbent assay.

33. **(Original)** The process according to claim 1 additionally comprising providing the cell expressing the membrane transport protein.

34. **(Cancelled)**

35. **(Original)** The process according to claim 1 additionally comprising fixing the cell.

36. **(Cancelled)**

37. **(Cancelled)**

38. **(Cancelled)**

39. **(Original)** The process according to claim 1 additionally comprising inducing translocation of the membrane transport protein to the plasma membrane.

40. **(Cancelled)**

41. **(Cancelled)**

42. **(Cancelled)**

43. **(Original)** The process according to claim 1 additionally comprising inducing resistance to translocation of the membrane transport protein in the cell.

44. **(Cancelled)**

45. **(Cancelled)**

46. **(Cancelled)**

47. **(Original)** The process of claim 1 comprising:

(a) determining the level of the membrane transport protein at the plasma membrane of a cell using a method comprising:

- (i) contacting a cell with a ligand that binds to an extracellular domain of the membrane transport protein for a time and under conditions sufficient for the ligand to bind to the membrane transport protein; and
- (ii) determining the level of ligand bound to the membrane transport protein;
- (b) determining the level of the membrane transport protein within another cell using a method comprising:
  - (i) permeabilizing or disrupting the other cell;
  - (ii) contacting the membrane transport protein within the cell with the ligand for a time and under conditions sufficient for the ligand to bind the membrane transport protein;
  - (iii) determining the level of ligand bound to the membrane transport protein; and
- (c) comparing the level of ligand detected at (a) (ii) and (b) (iii) to determine the level of the labeled membrane transport protein at the plasma membrane relative to the total level of labeled membrane transport protein.

48. **(Original)** The process according to claim 47 wherein the cells are isogenic or from the same cell line.

49. **(Cancelled)**

50. **(Currently amended)** The process according to claim ~~49~~ 47 or 48 wherein the cells are cultured under substantially similar conditions and wherein the level of the membrane transport protein at the plasma membrane of the cell and the level of membrane transport protein within the cell are each determined in a plurality of cells.

51. **(Original)** The process according to claim 50 additionally comprising normalizing the determined level of ligand bound to the membrane transport protein with regard to the number of cells in which the level of ligand bound to the membrane transport protein is determined.

52. **(Cancelled)**

53. **(Cancelled)**

54. **(Original)** A process for determining the level of a labeled GLUT4 protein or labeled mutant GLUT4 protein translocated to the plasma membrane of a cell, wherein said labeled mutant GLUT4 protein has a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein, said process comprising:

(a) determining the level of the labeled GLUT4 protein or labeled mutant GLUT4 protein at the plasma membrane of a cell expressing the labeled GLUT4 protein or labeled mutant GLUT4 protein using a method comprising:

(i) contacting the cell with a ligand that binds to the label for a time and under conditions sufficient for the ligand to bind to the labeled GLUT4 protein or labeled mutant GLUT4 protein; and

(ii) determining the level of ligand bound to the labeled GLUT4 protein or labeled mutant GLUT4 protein;

(b) determining the level of membrane transport protein within another cell expressing the labeled GLUT4 protein or labeled mutant GLUT4 protein using a method comprising:

(i) permeabilizing or disrupting the other cell;

(ii) contacting the labeled GLUT4 protein or labeled mutant GLUT4 protein within the cell with a ligand that binds to the label for a time and under conditions sufficient for the ligand to bind to the labeled GLUT4 protein or labeled mutant GLUT4 protein;

(iii) determining the level of ligand bound to the labeled GLUT4 protein or labeled mutant GLUT4 protein; and

(c) comparing the level of ligand detected at (a) (ii) and (b) (iii) to determine the level of the labeled GLUT4 protein or labeled mutant GLUT4 protein at the plasma membrane relative to the total level of labeled GLUT4 protein or labeled mutant GLUT4 protein.

55. **(Original)** A process for determining the level of a labeled GLUT4 protein or a labeled mutant GLUT4 protein translocated to the plasma membrane of a cell that is resistant to insulin induced GLUT4 translocation, wherein said labeled mutant GLUT4 protein has a reduced

rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein, said process comprising:

(a) contacting a plurality of cells expressing a labeled GLUT4 protein or a labeled mutant GLUT4 protein with an amount of insulin sufficient to induce resistance to insulin induced translocation for a time and under conditions sufficient to induce resistance to insulin induced GLUT4 translocation in the cell, wherein the cells are contacted with insulin in the absence of serum and wherein the cells are contacted with insulin for a period of time from about 24 hours to about 48 hours;

(b) determining the level of the labeled GLUT4 protein or labeled mutant GLUT4 protein at the plasma membrane of a cell at (a) using a method comprising:

(i) contacting the cell with a ligand that binds to the label for a time and under conditions sufficient for the ligand to bind to the labeled GLUT4 protein or labeled mutant GLUT4 protein; and

(ii) determining the level of ligand bound to the labeled GLUT4 protein or labeled mutant GLUT4 protein;

(c) determining the level of labeled GLUT4 protein or labeled mutant GLUT4 protein in another cell at (a) but not (b) using a method comprising:

(i) permeabilizing or disrupting the other cell;

(ii) contacting the labeled GLUT4 protein or labeled mutant GLUT4 protein within the cell with a ligand that binds to the label for a time and under conditions sufficient for the ligand to bind to the labeled GLUT4 protein or labeled mutant GLUT4 protein;

(iii) determining the level of ligand bound to the labeled GLUT4 protein or labeled mutant GLUT4 protein; and

(d) comparing the level of ligand detected at (b) (ii) and (c) (iii) to determine the level of the labeled GLUT4 protein or labeled mutant GLUT4 protein at the plasma membrane relative to the total level of labeled GLUT4 protein or labeled mutant GLUT4 protein.

56. **(Currently amended)** A process for determining the level of recycling of a membrane transport protein in a cell or a change in the level of recycling of a cell comprising:

(a) determining the level of the membrane transport protein translocated to the plasma membrane of a cell using the process according to ~~any one of~~ claims 1-~~to~~ 54;

(b) determining the level of the membrane transport protein translocated to the plasma membrane of another cell using the process according to ~~any one of~~ claims 1-~~to~~ 54, wherein the other cell is cultured for a longer period of time than the cell at (a); and

(c) comparing the level of the membrane transport protein translocated to the plasma membrane at (a) and (b) to thereby determine the level of recycling of the membrane transport protein in the cell, wherein a change in the level of the membrane transport protein translocated to the plasma membrane indicates a change in the level of recycling of a membrane transport protein.

57. **(Currently amended)** A process for determining a mutation in a nucleic acid encoding a mutant membrane transport protein that is capable of modulating translocation of said membrane transport protein, said ~~method~~process comprising:

(i**a**) determining the level of the mutant membrane transport protein translocated to the plasma membrane of a cell using the process according to ~~any one of~~ claims 1-~~to~~ 54; and

(ii**b**) determining the level of the wild-type form of the membrane transport protein translocated to the plasma membrane of a cell using the process according to ~~any one of~~ claims 1-~~to~~ 54,

wherein an enhanced or suppressed level of translocation of the membrane transport protein at (a) compared to (b) indicates that the nucleic acid comprises a mutation that is capable of modulating the level of level of translocation of the membrane transport protein to the plasma membrane.

58. **(Currently amended)** A process for determining an agent that modulates translocation of a membrane transport protein to the plasma membrane of a cell, said process comprising:

(a) determining the level of a membrane transport protein translocated to the plasma membrane of a cell in the absence of a candidate agent by performing the process according to ~~any one of~~ claims 1-~~to~~ 54;

(b) determining the level of the membrane transport protein translocated to the plasma membrane of a cell in the presence of the candidate agent by performing the process according to ~~any one of~~ claims 1 to 54, wherein a difference in the level of the membrane transport protein translocated to the plasma membrane of a cell at (a) compared to (b) indicates that the candidate agent modulates translocation of the membrane transport protein.

- (c) optionally, determining the structure of the candidate agent;
- (d) optionally, providing the name or structure of the candidate agent; and
- (e) optionally, providing, the candidate agent.

59. **(Original)** A process for determining a candidate compound for the treatment of insulin resistance comprising:

(a) determining the level of the labeled GLUT4 protein or the labeled mutant GLUT4 protein translocated to the plasma membrane of a cell in the absence of a candidate agent by performing the process according to claim 55, wherein said labeled mutant GLUT4 protein has a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein; and

(b) determining the level of the labeled GLUT4 protein or a labeled mutant GLUT4 protein translocated to the plasma membrane of another cell in the presence of the candidate agent by performing the process according to claim 55, wherein said labeled mutant GLUT4 protein has a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein and wherein a candidate agent that enhances the level of translocation of the labeled GLUT4 protein or a labeled mutant GLUT4 protein is a candidate agent for the treatment of insulin resistance.

- (c) optionally, determining the structure of the candidate agent;
- (d) optionally, providing the name or structure of the candidate agent; and
- (e) optionally, providing, the candidate agent.

60. **(Cancelled)**

61. **(Cancelled)**

62. **(Currently amended)** A process for manufacturing a medicament for the treatment of insulin resistance comprising:



(a) determining a candidate ~~agent~~compound for the treatment of insulin resistance using a process comprising:

(i) determining the level of the labeled GLUT4 protein or the labeled mutant GLUT4 protein translocated to the plasma membrane of a cell in the absence of a candidate agent by performing the process according to claim 55, wherein said labeled mutant GLUT4 protein has a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein; and

(ii) determining the level of the labeled GLUT4 protein or a labeled mutant GLUT4 protein translocated to the plasma membrane of another cell in the presence of the candidate agent by performing the process according to claim 55, wherein said labeled mutant GLUT4 protein has a reduced rate of recycling or transporter internalization compared to a wild-type form of the membrane transport protein and wherein a candidate agent that enhances the level of translocation of the labeled GLUT4 protein or a labeled mutant GLUT4 protein is a candidate agent for the treatment of insulin resistance.

(b) optionally, isolating the candidate agent;

(c) optionally, providing the name or structure of the candidate agent;

(d) optionally, providing the candidate agent; and

(e) ~~using the candidate agent in the manufacture~~ manufacturing of a medicament comprising the candidate agent~~for the treatment of insulin resistance.~~